## REMARKS

Applicant's amendments are submitted to correct various informalities and to claim embodiments of the invention.

Pursuant to the Notice to File Corrected Application Papers mailed on May 17, 2004, a formalities objection was raised to embedded figures. These figures now have been moved in the instant application to the proper location and a "description of drawing" section introduced using language directly from the case as filed.

This amendment also corrects typographical errors in several structural depictions of the background portion of the compounds herein, i.e., in the parental drug structures and more particularly in the "methoxy" part of the methoxyphosphonate nucleotide analogues that serve as the parental drugs for the novel compounds of this invention. These corrections are as follows:

(1). On page 4, lines 26-34, and page 20, line 17, all of the structures given for E are missing the group $CH_2O$ to the left of each structure, e.g., for the first one given as $-(CH_2)_2-$, the structure should be $-CH_2O(CH_2)_2-$. The same omission is found in claim 21.

(2). On page 7, line 29, the structure "$A-OH_2P(O)(OH)_2$" is a typographical error for $A-OCH_2P(O)(OH)_2$.

These errors occur in the part of the compounds which is derived from prior art, known compounds. For example, specification page 1, lines 16-18, recites by way of background that

"Many methoxyphosphonate nucleotide analogues are known. In general, such compounds have the structure $A-OCH_2P(O)(OR)_2$ where A is the residue of a nucleoside analogue and R independently is hydrogen...."

In addition, the specification refers to a large number of references containing disclosures of these prior art compounds (see at least specification page 1, line 19 and page 8, lines 5-8). All phosphonate compounds contain the methoxy linker to the phosphorus atom. All of these prior art compounds are *methoxy*phosphonate compounds, a term also recited numerous times in the specification.

Finally, none of the specific embodiments in the specification involve any linkage other than methoxy. Thus, it is apparent that the recitation on page 7 of the structure "A-$OH_2P(O)(OH)_2$" erroneously recites "$OH_2$" in place of $OCH_2$.

As a more direct alternative to adding the methoxy group to the individual E groups, applicants have elected to add the missing methoxy group to the structures to which E relates (structures (3), (4) and at the bottom of page 7, as well as claim 21),

This amendment adds no new matter.

Corresponding claims 1-5, 10-12, 14 and 17-18 in parent application serial number 09/909,560 had been rejected as obvious over or anticipated by Starrett *et al* . This reference teaches administering various prodrugs of the compound PMEA to rats, collecting urine and determining the amount of urinary PMEA as metabolite. The Office took the view that Starrett *et al* disclosed all features of the claimed method except for assaying metabolism in non-target tissue. This rejection is not believed to have been well founded.

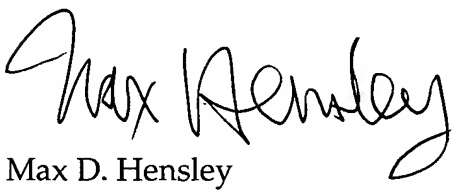
The claimed feature that Starrett *et al* fail to teach is "determining the relative activity" of the test prodrug in target and non-target tissue. In short, Starrett *et al* does not make any comparative study of metabolism in target versus non-target tissue. On the contrary, in collecting urine Starrett *et al* necessarily only determined whole body prodrug metabolism. Starrett et al. fail to teach or suggest the therapeutically important

observation by the inventors that the methoxyphosphonate nucleotide analogue class of agents can be targeted to certain tissues by selection of appropriate pro-functionalities. Targetting permits the drug to take up residence for extended periods in tissues most in need to therapeutic intervention. This in turn is believed to lead to dose and toxicity reductions. Accordingly, the claims expressly recite testing the prodrug in non-target tissue (this in fact could be the entire animal since the entire animal includes non-target tissue) and then in target tissue, e.g., peripheral blood lymphocytes. Prodrugs having the highest relative activity for target tissue then would be identified as a promising therapeutic prodrug candidate. Starrett et al. fails to teach or suggest the presently claimed invention.

An Information Disclosure Statement is submitted herewith. This IDS is the same one reviewed and initialed by Examiner Leary in the '207 parent.

This application is now believed to be in condition for allowance. Applicants would be grateful for an early Notice of Allowance.

Respectfully Submitted,



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Attachment: IDS
Substitute specification